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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,757	03/25/2004	Charles R. Yates	D6502	8644

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Benjamin Aaron Adler
ADLER & ASSOCIATES
8011 Candle Lane
Houston, TX 77071

EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/809,757	YATES ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4, 17, 21-23* is/are pending in the application.

4a) Of the above claim(s) *21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Election/Restrictions

1. Applicant's election with traverse of group II, claims 4 and 17 in the reply filed on 1/4/05 is acknowledged. The traversal is on the ground(s) that newly added claims 21-23 should be included in group II. However, these method claims would be properly placed in group I of the original restriction groupings. As noted in the original restriction requirement, the products of group I can be used in a variety of methods, such as in hybridization assays, nucleic acid purification assays and as capture probes attached to a solid support, and these two groups are separately classified.

2. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, as exemplified by the different classes and subclasses, restriction for examination purposes as indicated is proper. Further it would pose as serious burden on the examiner to search and examine both the products and the methods together because, a search for the inventions of the two groups would not be coextensive because a search indicating the process is novel or unobvious would not extend to a holding that the products themselves are novel or unobvious; similarly, a search indicating that the product is known or would have been obvious would not extent to a holding that the process is known or would have been obvious. Therefore, restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made FINAL.

3. Applicant is reminded that in the case of a restriction between products and methods of use, where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the

limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Sequence Listing

4. The CRF filed with this application has been entered into the STIC database. Prior to entry, the mandatory <140> heading was amended or added.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 4 and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Song et al. (AAPS PharmSci 2002; 4(4) article 29 (http://www.aapspharmsci.org), published October 2, 2002).

Song et al. teach primers having the sequences of SEQ ID NO: 1, SEQ ID NO: 2, and SEQ ID NO: 3. Specifically, referring to Table 1 of the reference, primer 3435W is identical to instant SEQ ID NO: 1, primer 3435M is identical to SEQ ID NO: 2, and primer 3435R is identical to SEQ ID NO: 3. With regard to claim 4 in particular, the recitation of a "kit" in the preamble of claim 1 is interpreted as intended use language as it does not appear to provide any structural limitation on the claim. With regard to claim 17, these are each isolated DNA molecules. Thus, the reference anticipates the rejected claims.

It is noted that the authorship of the Song et al. reference is distinct from the inventorship of the instant application and that this rejection may be overcome by the filing of a 132 Katz-type declaration.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Song et al. (Clinical Pharmacology & Therapeutics, volume 71, Number 2, February 2002, p. P103, abstract WPIII-100) in view of Hoffmeyer et al. (PNAS, Vol. 97, No. 7, pages 3473-3478, March 28, 2000), GenBank M14758 (GI: 187468, 3 December 1999) and Okimoto et al. (BioTechniques, Vol. 21, pages 20-26, July 1996).

Song et al. teach an isolated nucleic acid primer that is used in allele specific real-time PCR-based genotyping to detect the C3435T polymorphism within the human MDR1 gene. Song et al. specifically teach that in the primers an additional nucleotide mismatch at the –3 position from the 3' end of each allele specific primer was used to abrogate non-specific PCR amplification. Song et al. do not teach the particular sequence of the primer, nor do they provide sequence context for the identification of the C3435T polymorphism.

Hoffmeyer et al. provide the sequence polymorphism for the C3435T polymorphism within the MDR1 gene, particularly referring to GenBank record M14758 as containing the full length sequence of the gene (see Table 1 and description).

The GenBank record provides the cDNA for the MDR1 gene, as noted by Hoffmeyer et al. Aligning the context sequence given in Table 1 of Hoffmeyer et al., the polymorphic position is identified as being at position 3859 of the sequence taught in the GenBank record. Further, the GenBank record teaches in the comments section of the record that there is a C/T polymorphism at position 3859 of this sequence. Instant SEQ ID NO: 1 is identical to nucleotides 3839-3859 of the sequence taught in the GenBank record, except for a single nucleotide mismatch at the –3 position from the 3' end, of this fragment, which is the position two nucleotides downstream of the polymorphic site. Instant SEQ ID NO: 2 is identical to nucleotides 3839-3859 of the sequence taught in the GenBank record, except for a single nucleotide mismatch at the –3 position from the 3' end, of this fragment, which is the position two nucleotides downstream of the polymorphic site, and the C is replaced with a T at the polymorphic site.

Okimoto et al. provide teaching about allele specific PCR and exemplify the use of primers that contain added mismatches at the –3 position from the 3' end in the three prime end. In the allele specific primers used by Okimoto et al., the polymorphic position is aligns with the 3' terminus of the primers, and the allele specific primers are twenty and twenty-six nucleotides (see Table 1, for example).

Thus, given the specific teaching of Song et al., and the significant guidance in the prior art teachings of Hoffmeyer et al., the GenBank record, and Okimoto et al., it would have been

prima facie obvious to have modified the teachings of Song et al. so as to have created allele specific primers with a single mismatch at the –3 position from the 3' end for the detection of the MDR1 C3435T polymorphism. One would have been motivated to create such a primer by the express teaching of Song et al. that such a primer abrogates non-specific PCR amplification. Following the guidance of the prior art, a number of different primers could be made (i.e., a variety of lengths, and with three possible alternative nucleotides at the at the –3 position from the 3' end of the primer, the MDR1 sequence normally has an "A" at this position). However, each of these primers would be obvious variants of one another, including the primers consisting of instant SEQ ID NO: 1 and SEQ ID NO: 2 and of the primer taught in the prior art in that they would all have the general structure specifically taught by Song et al. and would be expected to function as equivalents for the detection of the C3435T polymorphism.

Therefore, in view of the teachings of the prior art, the claimed invention is *prima facie* obvious.

10. Claims 4 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Song et al. (Clinical Pharmacology & Therapeutics, volume 71, Number 2, February 2002, p. P103, abstract WPIII-100) in view of Hoffmeyer et al. (PNAS, Vol. 97, No. 7, pages 3473-3478, March 28, 2000), GenBank AC005068 (GI: 10122135, 7 October 2000) and Okimoto et al. (BioTechniques, Vol. 21, pages 20-26, July 1996).

Song et al. teach an isolated nucleic acid primer that is used in allele specific real-time PCR-based genotyping to detect the C3435T polymorphism within the human MDR1 gene. Song et al. specifically teach that in the primers an additional nucleotide mismatch at the –3 position from the 3' end of each allele specific primer was used to abrogate non-specific PCR

amplification. Song et al. do not teach the particular sequence of the primer, nor do they provide sequence context for the identification of the C3435T polymorphism.

Hoffmeyer et al. provide the sequence polymorphism for the C3435T polymorphism within the MDR1 gene, teaching that it is within exon 26 of the gene (see Table 1 and description). Hoffmeyer et al. also specifically refer to GenBank record AC005068 as teaching the genomic DNA sequence for exons 8-28 of the MDR1 gene.

As noted by Hoffmeyer, the GenBank record provides the sequence for exon 26 of for the MDR1 gene. Aligning the context sequence given in Table 1 of Hoffmeyer et al., the polymorphic position is identified as being at position 43268 of the sequence taught in the GenBank record (the sequence gives the complement of the context sequence given in Hoffmeyer et al. Instant SEQ ID NO: 1 is identical to the complement of nucleotides 43268-43288 of the sequence taught in the GenBank record, except for a single nucleotide mismatch at the –3 position from the 3' end, of this fragment, which is the position two nucleotides downstream of the polymorphic site. Instant SEQ ID NO: 2 is identical to the complement nucleotides 43268-43288 of the sequence taught in the GenBank record, except for a single nucleotide mismatch at the –3 position from the 3' end, of this fragment, which is the position two nucleotides downstream of the polymorphic site, and the C is replaced with a T at the polymorphic site. Instant SEQ ID NO: 3 is identical to nucleotides 43155-43175 of the sequence taught in GenBank record.

Okimoto et al. provide teaching about allele specific PCR and exemplify the use of primers that contain added mismatches at the –3 position from the 3' end in the three prime end. In the allele specific primers used by Okimoto et al., the polymorphic position is aligns with the

3' terminus of the primers, and the allele specific primers are twenty and twenty-six nucleotides (see Table 1, for example). Okimoto et al. teach that one of the advantages of using an additional mismatch within a primer is that it allows for the amplification of "shorter" PCR products that traditional processes (p. 22, first column), and teach that they have used mismatched primers to amplify products between 91 and 163 base pairs in length (p. 24, first column).

Thus, given the specific teaching of Song et al., and the significant guidance in the prior art teachings of Hoffmeyer et al., the GenBank record, and Okimoto et al., it would have been prima facie obvious to have modified the teachings of Song et al. so as to have created allele specific primers with a single mismatch at the –3 position from the 3' end for the detection of the MDR1 C3435T polymorphism. One would have been motivated to create such primers by the express teaching of Song et al. that such a primer abrogates non-specific PCR amplification. Further, it would have been prima facie obvious to select an additional reverse primer to use in PCR amplification with the allele specific primer. Following the guidance of the prior art, a number of different primers could be made (i.e., a variety of lengths, and with three possible alternative nucleotides at the at the –3 position from the 3' end of the primer, the MDR1 sequence normally has an "A" at this position). Each of these primers would be obvious variants of one another, including the primers consisting of instant SEQ ID NO: 1 and SEQ ID NO: 2 and SEQ ID NO: 3, and they would be variants the primers taught in the prior art in that they would all have the general structure specifically taught by Song et al. and would be expected to function as equivalents for the detection of the C3435T polymorphism. With regard to the reverse primer, it would have been obvious to select any primer that would function to amplify DNA with the

allele specific primers and that would create "smaller" PCR products as suggested by Okimoto et al., such as a primer that comprises SEQ ID NO: 3 which clearly falls within this range. It is further noted that the kit of claim 4 encompasses any primers within it that comprise the recited sequences allowing a large degree of variability with regard to even the length of the claimed primers themselves.

Therefore, in view of the teachings of the prior art, the claimed invention is *prima facie* obvious.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday through Wednesday, from 9:00 AM until 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached by calling (571) 272-0745.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Juliet C. Switzer
Primary Examiner
Art Unit 1634

March 15, 2005